Full Text AR-94-004

BASIC RESEARCH ON FIBROMYALGIA

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National Institute of Arthritis and Musculoskeletal and Skin Diseases

Letter of Intent Receipt Date: December 15, 1993
Application Receipt Date: February 10, 1994

PURPOSE

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) invites applications for basic research on the pathogenesis of fibromyalgia (FM). The goal of the Request for Applications (RFA) is to promote research that will improve our understanding of the disease and will identify critical processes and mediators of disease that could be used to establish a rational basis for new and effective treatments. Multidisciplinary approaches that combine molecular and cellular biology techniques with neuroendocrinology, immunology, and pharmacology research are strongly encouraged.

HEALTHY PEOPLE 2000

The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2000," a PHS-led national activity for setting priority areas. This RFA, Basic Research on Fibromyalgia, is related to the priority area of chronic disabling conditions. Potential applicants may obtain a copy of "Healthy People 2000" (Summary Report: Stock No. 017-001-00474-0 or "Healthy People 2000" (Summary Report: Stock No. 017-001-00473-1) through the Superintendent of Documents, Government Printing Office, Washington, DC 20402-9325 (telephone 202-783-3238).

ELIGIBILITY REQUIREMENTS

Applications may be submitted by domestic and foreign, for-profit and non-profit organizations, public and private, such as universities, colleges, hospitals, laboratories, units of State and local governments, and eligible agencies of the Federal government. Applications from minority individuals and women are encouraged. Foreign institutions are not eligible for First Independent Research Support and Transition (FIRST) (R29) award.

MECHANISM OF SUPPORT

This RFA will use the National Institutes of Health (NIH) individual research grant (R01), FIRST (R29) awards, and interactive research project grants (IRPG) mechanisms. IRPGs are further described in the NIH Guide, Vol. 22, No. 16, April 23, 1993. Responsibility for the planning, direction, and execution of the proposed project will be solely that of the applicant. The total project period for applications submitted in response to the present RFA may not exceed five years. The anticipated award date is September 30, 1994. Because the nature and scope of the research proposed in response to this RFA may vary, it is anticipated that the size of an award will also vary. This RFA is a one time solicitation. Future unsolicited competing continuation applications will compete with all investigator initiated applications and be reviewed according to customary peer review procedures.

Applicants from institutions that have a General Clinical Research Center (GCRC) funded by the NIH National Center for Research Resources may wish to identify the GCRC as a resources for conducting the proposed research. If so, a letter of agreement from either the GCRC program director or Principal Investigator could be included within the application.

FUNDS AVAILABLE

The estimated funds (total costs) available for the first year of support for the entire program is 1.4 million dollars. Funding is contingent upon receipt of scientifically meritorious applications. The NIAMS expects to fund five to seven new awards.

RESEARCH OBJECTIVES

Background

Fibromyalgia is a disorder characterized by widespread pain and multiple, characteristic, tender points. Fibromyalgia is associated with sleep disturbances, particularly non-restorative sleep, morning stiffness, aggravation by lower temperatures and amelioration by exercise. The precise frequency and natural history of fibromyalgia are unknown, but the disorder may affect about two to three percent of the population of the United States, and the majority of affected individuals are women. Fibromyalgia tends to overlap with a number of disorders, including irritable bowel and bladder syndromes, frequent headaches, and chronic fatigue syndrome. In 1990, the American College of Rheumatology published classification criteria for fibromyalgia. These criteria provide a uniform basis for classifying the cases and will be invaluable in conducting research in this area.

Although progress has been made in the identification and differential diagnosis of the disease, the lack of knowledge about the causes and mechanisms of the disease have limited the available treatments to empirical therapies that afford only modest clinical improvement. Future progress in the treatment of fibromyalgia will require greater and detailed understanding of the molecular pathogenetic mechanisms. The current status and future direction of fibromyalgia research was the subject of a Workshop sponsored by the National Institute of Arthritis and Musculoskeletal and Skin Diseases held on May 19, 1993. The Workshop brought together a group of clinicians and scientists working in the field of fibromyalgia that developed a comprehensive list of future research activities in fibromyalgia. A summary of this Workshop will be published in the Journal of Musculoskeletal Pain. Basic research on the pathogenesis of fibromyalgia was identified as one critical area of future emphasis and is the focus of the current solicitation.

The areas of research interest include, but are not limited to:

o Development of in vivo or in vitro systems that will allow analysis of biochemical and functional abnormalities observed in fibromyalgia;

o Family and genetic studies of fibromyalgia syndrome;

o Mechanisms of neurohormonal dysregulation in fibromyalgia, including alterations of the hypothalamic-pituitary-adrenal axis;

o Elucidation of pathophysiological and neurochemical mechanisms related to pain associated with fibromyalgia, including altered pain threshold and the existence of localized tender points;

o Studies on the mechanisms that mediate the relationship and overlap between fibromyalgia, irritable bowel, chronic fatigue syndrome and other chronic conditions;

o Studies on the role of infections in the induction or aggravation of fibromyalgia, the mechanisms of induction and the host factors that predispose to development of symptoms;

o Studies of sleep disturbances in fibromyalgia and their relationship to neurochemical, endocrine, biochemical immune or chronobiologic alterations to abnormalities of the neuroendocrine and immune system in fibromyalgia.

This list is illustrative and not exclusive or restrictive. Applications combining multidisciplinary approaches and applications that include collaborations between investigators with expertise in rheumatology and scientists with expertise in the disciplines of pharmacology, biochemistry, cellular biology, endocrinology and neurology are strongly encouraged. The application of current paradigms and technical approaches in those fields to the study of fibromyalgia are also highly recommended.

STUDY POPULATIONS

SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH policy is that applicants for NIH clinical research grants and cooperative agreements are required to include minorities and women in study populations so that research findings can be of benefit to all persons at risk of the disease, disorder or condition under study; special emphasis must be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented

in clinical research, particularly in proposed population-based studies, a clear compelling rationale must be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues must be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information must be included in the form PHS 398 (rev. 9/91) in Sections 1-4 of the Research Plan AND summarized in Section 5, Human Subjects. Applicants are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans [including American Indians or Alaskan Natives], Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research is defined as human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including, but not limited to, clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

LETTER OF INTENT

Prospective applicants are asked to submit, by December 15, 1993, a letter of intent that includes a title of the proposed research, the name, address, and telephone number of the Principal Investigator, the identities of other key personnel and participating institutions, and the number and title of the RFA in response to which the application may be submitted.

Although a letter of intent is not required, is not binding, and does not enter into the review of subsequent applications, the information that it contains allows NIAMS staff to estimate the potential review workload and to avoid conflict of interest in the review.

The letter of intent is to be sent to Dr. Susana A. S. Sztein at the address listed under INQUIRIES.

APPLICATION PROCEDURES

The research grant application form PHS 398 (rev. 9/91) is to be used in applying for these grants. These forms are available at most institutional offices of sponsored research; from the Office of Grants Information, Division of Research Grants, National Institutes of Health, 5333 Westbard Avenue, Room 449, Bethesda, MD 20892, telephone 301/435-0714.

The RFA label available in the PHS 398 (rev. 9/91) application form must be affixed to the bottom of the face page of the application. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2a of the face page of the application form and the YES box must be marked.

Applications for the FIRST Award (R29) must include at least three sealed letters of reference attached to the face page of the original application. FIRST (R29) applications submitted without the required number of reference letters will be considered incomplete and will be returned without review.

Submit a signed, typewritten original of the application, including the Checklist, and three signed, photocopies, in one package to:

Division of Research Grants
National Institutes of Health
Westwood Building, Room 240
Bethesda, MD 20892**

At the time of submission, two additional copies of the application must also be sent to:

Tommy Broadwater, Ph.D.
Review Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 406
Bethesda, MD 20892
Telephone: (301) 594-9979
FAX: (301) 594-9673

Applications must be received by February 10, 1993. If an application is received after that date, it will be returned to the applicant without review. The Division of Research Grants (DRG) will not accept any application in response to this announcement that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The DRG will not accept any application that is essentially the same as one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an introduction addressing the previous critique.

REVIEW CONSIDERATIONS

Upon receipt, applications will be reviewed for completeness by DRG and responsiveness by the NIAMS staff. Incomplete applications will be returned to the applicant without further consideration. If the application is not responsive to the RFA, NIAMS staff will contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next review cycle.

Applications may be triaged by an ICD peer review group on the basis of relative competitiveness. The NIH will withdraw from further competition those applications judged to be non-competitive for award and notify the applicant Principal Investigator and institutional official.

Those applications judged to be competitive will undergo further scientific merit review. Those applications that are complete and responsive will be evaluated in accordance with the criteria stated below for scientific/technical merit by an appropriate peer review group convened by the NIAMS. The second level of review will be provided by the National Arthritis and Musculoskeletal and Skin Diseases Advisory Council.

Review criteria for this RFA are generally the same as those for unsolicited research grant applications.

o scientific, technical, or clinical significance and originality of proposed research;

o appropriateness and adequacy of the experimental approach and methodology proposed to carry out the research;

o qualifications and research experience of the Principal Investigator and staff;

o availability of the resources necessary to perform the research;

o appropriateness of the proposed budget and duration in relation to the proposed research;

AWARD CRITERIA

The anticipated date of award is September 30, 1994.

Awards will be based upon the following criteria:

o scientific merit
o availability of funds
o programmatic priorities of the funding ICD
o responsiveness to the RFA

INQUIRIES

Written and telephone inquiries concerning this RFA are encouraged.
The opportunity to clarify any issues or questions from potential applicants is welcome.

Direct inquiries regarding programmatic issues and address the letter of intent to:

Susana A. S. Sztein, M.D.
Rheumatic Diseases Branch
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 405
Bethesda, MD 20892
Telephone: (301) 594-9953
FAX: (301) 594-9673

Direct inquiries regarding fiscal matters to:

Mara DeKemper
National Institute of Arthritis and Musculoskeletal and Skin Diseases
Westwood Building, Room 722
Bethesda, MD 20892
Telephone: (301) 594-7508
FAX: (301) 594-9950

Schedule

Letter of Intent Receipt Date: December 15, 1993
Application Receipt Date: February 10, 1993
Initial Review: June/July 1994
Second Level Review: September 1994
Anticipated Award Date: September 30, 1994

AUTHORITY AND REGULATIONS

This program is described in the Catalog of Federal Domestic Assistance No. 93.361,. Awards are made under authorization of the Public Health Service Act, Title IV, Part A (Public Law 78-410, as amended by Public Law 99-158, 42 USC 241 and 285) and administered under PHS grants policies and Federal Regulations 42 CFR 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

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